

endemic, food handlers, male homosexuals, injecting drug users, and day care center children and staff.

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An Outbreak of Measles at an International Sporting Event with Airborne Transmission in a Domed Stadium

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An outbreak of measles occurred in conjunction with the International Special Olympics Games in the Minneapolis-St. Paul metropolitan area during July 1991. Sixteen outbreak-associated cases of measles were reported among US residents from seven states, with 9 additional cases resulting from subsequent transmission. The primary case was a track and field athlete from Argentina. Transmission occurred in three settings: the opening ceremonies in a domed stadium, track and field events, and first aid stations. Eight secondary cases had their only potential exposure at the opening ceremonies; 2 of these cases were unrelated spectators sitting in the same section of the upper deck >30.5 m above the athlete's entrance. These findings demonstrate that the risk of indigenous measles transmission associated with international events in the United States must be considered, even in areas without recent measles activity. Moreover, the dynamic airborne transmission of measles illustrates the potential for transmission in the absence of a recognized exposure.

International sporting events provide the potential for efficient and widespread transmission of measles. Athletes and

spectators from countries where outbreaks are occurring or where measles is endemic may travel during their incubation period when they are infectious, resulting in exposure to people from areas where the disease is uncommon. Mass gatherings of spectators, trainers, and medical support personnel further increase the risk of transmission to susceptible persons in a confined environment [1-4]. The International Special Olympics (ISO) Games were held in the Minneapolis-St. Paul (Twin Cities) metropolitan area 19-26 July 1991; 6058 athletes from all 50 states and 93 nations participated. The games also were attended by 40,000 support staff and

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~150,000 spectators. The week-long competition began with opening ceremonies on 20 July in a domed stadium in Minneapolis. This event involved all athletes and their coaches and ~55,000 spectators. In addition to athletic competition, there were adjunct social events for athletes, coaches, and families.

On 6 August 1991, the Minnesota Department of Health (MDH) was notified by 2 Twin Cities physicians of measles in 2 Minnesota residents who had been involved with the ISO. Onset of rash was 14 and 15 days after their participation. In addition, epidemiologists from two state health departments contacted MDH on 7 August to report additional measles in ISO participants.

Methods

Case definition. An outbreak-associated case of measles was defined as a person who had involvement with the ISO and who developed a rash illness lasting ≥ 3 days with cough, coryza, or conjunctivitis and a temperature $> 38.3^\circ\text{C}$. A confirmed case required demonstration of measles-specific IgM antibody or a ≥ 4 -fold rise in measles antibody titer. A probable case was a person who met the clinical case definition but did not have laboratory confirmation [5]. Incubation periods for outbreak-associated cases were calculated from the date of presumed exposure to the source case to the date of rash onset.

Surveillance. All state health departments and Special Olympics chapters were notified of the occurrence of measles at the ISO and asked to report outbreak-associated measles cases to MDH. The ISO office in Washington, DC, was asked to notify international delegations of the outbreak. A local press release issued by MDH described the outbreak and informed volunteers and spectators at the games that they might have been exposed to measles. A month after the initial notification, follow-up telephone calls were made to all state health departments and Special Olympics chapters to identify cases. Clinical, epidemiologic, and laboratory data were collected on all confirmed measles illnesses in ISO participants and all suspected secondary and community-acquired measles illnesses related to the outbreak. Cases were interviewed by local health officials to ascertain potential sources of exposure.

Medical records review. To identify potential source case(s), ~4000 medical records from participant visits to first aid sta-

tions during the ISO were reviewed for history of cough, coryza, conjunctivitis, fever, and rash. Additional demographic and activity data were collected and hospital emergency room records were reviewed for all measles-like illnesses. After a probable source case was identified, his family and physician were interviewed in their home country (i.e., Argentina).

Statistical analysis. Odds ratios (ORs) and 95% confidence intervals (CIs) were determined by standard univariate analyses. Differences in proportions were tested using the χ^2 or Fisher's exact test [6].

Results

Surveillance. Sixteen outbreak-associated secondary measles cases were reported in athletes (7), spectators (3), and volunteers (6); all were US citizens. We were unable to follow-up with international delegations to ascertain information on transmission of measles to participants from other nations. The median age of reported cases was 21 years (range, 16–30); 14 (87%) were male. Dates of rash onset for the outbreak-associated cases were 1–13 August 1991 (figure 1). Nine additional cases were identified that occurred after the measles virus was transmitted by outbreak-associated cases to persons not directly involved with the ISO games.

Of the 16 outbreak-associated secondary and 9 subsequent measles cases, 15 had positive serology for measles IgM antibody. In 2 cases, measles infection was confirmed by a ≥ 4 -fold rise in measles antibody in acute and convalescent sera. Eight cases did not have laboratory confirmation but were epidemiologically linked to the ISO games or to another outbreak-associated case.

Twenty-four cases (96%) were age-eligible to have been vaccinated; the remaining case occurred in a 5-month-old child. Six (25%) of the age-eligible cases had documentation of one dose of measles vaccine; this included 1 (14%) of 7 athletes, 2 of 6 volunteers, 2 of 3 spectators, and 1 of the 8 subsequent cases. Thus, 18 of the 24 cases involved in this outbreak were potentially preventable.

Medical records review. Several measles-like illnesses were identified by review of participants' medical records; however, only 1 person had symptoms that met the clinical case definition: a 12-year-old boy athlete from Argentina. He

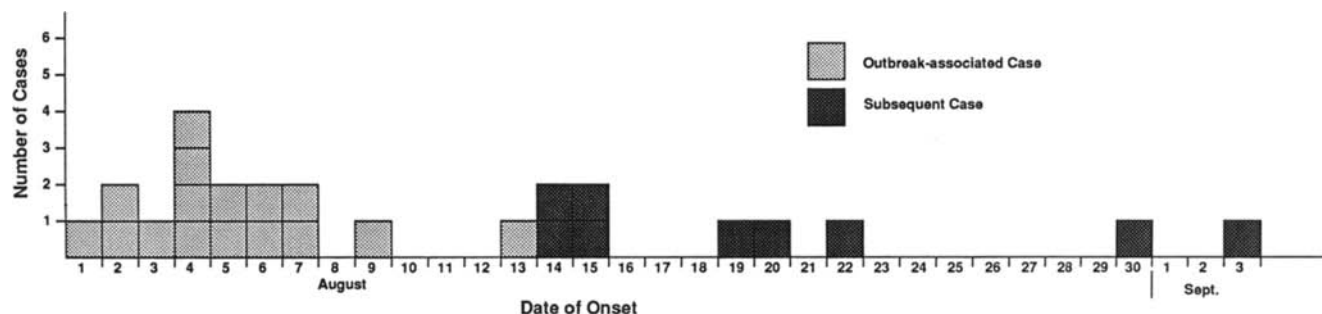


Figure 1. Measles cases by date of onset beginning with International Special Olympics, Minnesota, 1991.

was seen at a Twin Cities hospital emergency room on 24 July 1991 and had a 5-day history of cough and conjunctivitis, a fever of 39.8°C, and morbilliform rash. His personal physician in Argentina reported that when the boy arrived in the United States he complained of a dry cough and conjunctivitis. On 22 July 1991, a morbilliform rash began around his neck and descended caudally to the trunk and extremities; the rash lasted until 25 July. His mother reported that he had previously been vaccinated against measles and had a history of measles (although neither was confirmed by a physician). According to the boy's physician, an epidemic of measles was occurring in Argentina in July 1991.

Transmission. Transmission to ISO participants likely occurred in three settings: track and field events, first aid stations, and the opening ceremonies. The median incubation period from presumed exposure to onset of rash was 14 days (range, 11–22; figure 2). The primary case participated in track and field events on 21 and 22 July. Five cases were likely exposed while attending these events.

Three cases occurred among first aid workers. One volunteer restocked supplies and had been at all of the first aid stations. The other 2 volunteers had been at first aid stations near the source case's dormitory. Of the 40,000 support staff, 800 were first aid volunteers. Three of the 800 first aid volunteers acquired measles compared with 3 of the other 39,200 volunteers (OR, 49.2; 95% CI, 8.0–304.0; $P < .001$).

The other 8 cases among ISO participants were likely exposed at the opening ceremonies on 20 July in the Hubert H. Humphrey Metrodome, a domed stadium. Four of these cases were athletes; 1 was a translator. There were no known direct contacts between the source case and these 5 participants; none resided at his dormitory. Contact at one of the many adjunct activities planned for the athletes may have occurred; however, the opening ceremonies was the only known event in which all participated.

One subject who acquired measles set up equipment before the opening ceremonies. He remained on site and greeted athletes as they entered the stadium, ensuring direct face-to-face contact with the source case. Two cases occurred in unrelated spectators whose only potential source of expo-

sure at the ISO was attendance at the opening ceremonies. Both sat in the same section of the upper deck of the stadium, >30.5 m above the athletes' entrance. Rash onset followed 15–18 days after the opening ceremonies. These 2 spectators had no other known measles exposures. Both were Minnesota residents; the last reported measles case in Minnesota was 3 months earlier and was imported from outside the United States.

At least 9 cases of subsequent spread of measles occurred in three states as a result of transmission from the 16 outbreak-associated cases. These cases were in persons who ranged in age from 6 months to 30 years (median, 16 years). Six of the 9 were males. Five cases acquired measles directly from an outbreak-associated case. These 5 served as the source of infection for another 4 persons.

In addition to the 16 outbreak-associated secondary cases and 9 subsequent cases of measles identified, 4 community-acquired measles cases with no known exposure to the ISO games or outbreak-associated cases were reported in Minnesota after the games. These 4 had rash onset ~2 weeks after the outbreak-associated cases. Three additional cases were subsequently reported among contacts of these cases. No endemic measles transmission had been reported in Minnesota since the previous March, a period of ~120 days. These 7 cases cannot be directly linked to the ISO games but had no other reasonable sources of exposure.

Stadium air circulation. A pressurized airflow system is used to maintain the inflation of the collapsible dome ceiling. Air is taken from the main floor and recirculated to the upper decks by way of vents, duct work, and fans. Outside air is also drawn into the dome. The amount of outside air used depends upon the air temperature and humidity. On cold or hot days less outside air is exchanged and more is recirculated to limit heating or cooling costs. On the day of the opening ceremonies, the maximum temperature in Minneapolis was 30°C, making recirculation of inside air very likely. Precise operating conditions for specific events are not recorded and information regarding airflow during the opening ceremonies was not available. Under any circumstances, ~6995 m³ of stadium air is exchanged or recirculated per

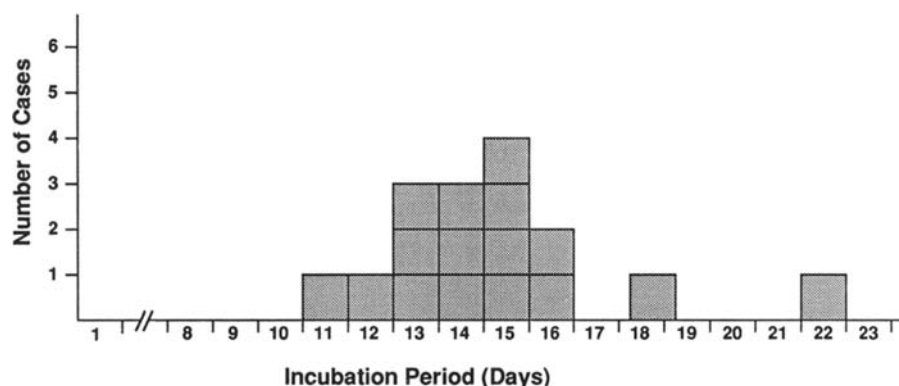


Figure 2. Primary measles cases by incubation period (days from exposure to rash onset), International Special Olympics, Minnesota, 1991.

minute during an event. The volume of air that can be accommodated by a single vent is 699.5 m³/min. Studies of nitrogen dioxide and carbon monoxide levels during motorized sporting events at the dome suggest that airflow throughout the dome is uneven (MDH, unpublished data). Air circulation is greatest near vents and lowest on the concourse level. In addition to proximity to vents, use of fans during events also affects airflow to a particular section. It is estimated that 7 of the 18 fans were in use on the night of the opening ceremonies. If fans near the upper-deck section where the 2 cases were seated were not in use, air from the athletes' entrance would have been pushed in that direction.

Discussion

This outbreak led to ≥ 25 measles cases and as many as three generations of measles transmission. Our results highlight the ease with which measles infection can be transmitted throughout the world despite limiting factors, such as a single source case, season of the year, and the immunization status of participants. Our findings suggest that this outbreak resulted from importation of measles in a 12-year-old boy from Argentina. Additional source cases would have exposed a larger and more diverse group of participants.

Measles occurred in spectators seated in an upper-deck section of a stadium, suggesting that the measles virus was transmitted in a turbulent airflow through the ventilation system rather than via concentric dispersion of the virus throughout the stadium. Previously documented airborne measles transmission has occurred in smaller settings, such as physicians' offices or via school ventilation systems [7, 8]. However, the crowded environment of indoor sporting events provides ideal conditions for respiratory transmission of a virus with a low infectious dose (e.g., measles).

Even with virtual elimination of measles from the United States, importation of measles will continue. Measles transmission is a function of local immunization levels and length of exposure and mixing. Transmission of measles in Minnesota during this outbreak was limited, considering the multiple opportunities for mixing and exposure. This can be attributed to fairly high immunization levels throughout the state. Although a 1992 survey of kindergartners indicated that only 82.5% of 2-year-old children in the state had received the measles-mumps-rubella vaccine, nearly all (98%) school-age children have been immunized (MDH, unpublished data). We believe that in the future, the success of community-wide measles immunization efforts should be measured by their ability to withstand importation of disease with no or limited disease transmission.

The occurrence of measles in 6 persons known to have received a single dose of vaccine plus a seventh said to have received one dose (the source case), suggests that the estimated 5%–10% vaccine failure rate provides enough susceptible persons to allow for sustained measles transmission in certain settings [9]. The two national advisory bodies for im-

munization policy recommended a routine two-dose measles vaccination schedule in 1989 [10, 11]. Complete implementation of this two-dose policy should reduce vaccine failure and subsequent outbreaks in immunized populations.

This outbreak also demonstrates the importance of ensuring adequate immunization of participants at international sporting events against measles and other vaccine-preventable diseases. The Centers for Disease Control and Prevention recommends that delegates, staff, volunteers, and visitors be appropriately vaccinated against vaccine-preventable diseases before attending an international event [1]. Vaccination records should be maintained in data bases that include birth date, home address (including country), telephone number, and vaccination histories. Also, participants ≤ 18 years old should have authority to designate an accompanying adult to authorize medical intervention [1].

During planning of the ISO, importation of disease into Minnesota by athletes and staff was not considered. All planning for infectious disease prevention focused on diseases acquired through direct contact with blood and body fluids. The potential for transmission of respiratory transmitted vaccine-preventable disease was not considered by ISO planners, and up-to-date immunization records were not a requirement for participation [12]. In the future, athletic governing bodies and local organizing officials should consult public health officials in advance of such events to establish recommendations and guidelines that take public health concerns into account [4]. Efforts to ensure adequate immunization of staff and participants are needed to reduce the risk of future outbreaks.

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Elevated Levels of Activities of β -Hexosaminidase and α -Mannosidase in Human Immunodeficiency Virus-Infected Patients

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To determine their value as markers of the clinical stage of human immunodeficiency virus (HIV) disease, plasma activities of lysosomal glycosidases were determined in the plasma of 97 HIV-infected patients: molecular forms of cathepsin D were characterized by Western blot to examine the mode of enzyme release. In patients with Centers for Disease Control and Prevention stage II and III of HIV disease, plasma activity of β -hexosaminidase was significantly increased. In patients with stage III infection, α -mannosidase activity was also significantly increased and cathepsin D was elevated and present only in its premature form. Thus, determination of plasma activities of β -hexosaminidase and α -mannosidase in HIV-positive persons may be useful for distinguishing the clinical stage of disease. The elevation of precursors of cathepsin D in patients with stage III HIV disease indicates that secretion of lysosomal enzymes rather than leakage of enzymes from damaged cells is markedly elevated.

Early diagnosis of the stage of human immunodeficiency virus (HIV) infection is important if therapeutic interventions are to be implemented and evaluated [1]. CD4⁺ cell count is currently the surrogate marker that most closely correlates with HIV disease progression [2, 3]. However, individual CD4⁺ lymphocyte counts are highly variable over time, and considerable overlap of CD4⁺ cell counts among the clinically defined stages of HIV infection has been found [3].

Different lysosomal enzymes, which play an important role in normal metabolic turnover, degradation of hormones, and defense against infection, have been described [4-6]. They are synthesized as precursors of higher molecular mass and subsequently processed to mature forms [7-9]. The newly synthesized enzymes are recognized by a specific receptor, the mannose-6-phosphate receptor [10], which is highly concentrated in membranes of the Golgi compartment, and binds the mannose-6-phosphate recognition marker, which is added to the lysosomal enzymes in the *cis*-

Golgi elements. This mechanism ensures that the enzymes are sorted out of the flow of other proteins synthesized by the cells. The enzymes remain bound to this mannose-6-phosphate receptor until they reach an acidified compartment, where low pH induces their dissociation from the receptor.

In the present study, we determined activities of lysosomal enzymes in the plasma of 97 HIV-infected persons and analyzed these data with respect to the patients' clinical stage of the disease. Furthermore, we described the molecular forms of cathepsin D to provide information on release mechanisms of these proteins in HIV-infected persons.

Materials and Methods

Patients. Ninety-seven HIV-infected patients were classified according to their disease status using the 1993 Centers for Disease Control and Prevention (CDC) classification system [11]: Stage I includes clinical categories A1, A2, and B1; stage II includes A3, B2, and B3; stage III includes C1-3. The controls were 30 healthy HIV-negative laboratory workers and hospital personnel and were designated stage 0. Patients were carefully examined to rule out other diseases, such as diabetes mellitus and kidney disease, and active infection with hepatitis viruses, which can elevate serum levels of hydrolases. Patients with diabetes mellitus were identified with an oral glucose tolerance test. Kidney disease and active infection with hepatitis viruses were

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